PICTORIAL REVIEW

Atypical location of germinoma in basal ganglia in adolescents: radiological features and treatment outcomes

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ABSTRACT. The objective of this work is to describe the imaging findings, clinical profile and treatment response in four Chinese adolescent patients presenting with ectopic germinoma arising from basal ganglia. The clinical presentation, treatment regimens and the imaging findings at presentation and after treatment were described upon retrospective review of four Chinese adolescent patients. CT of the brain showed mixed solid cystic mass lesions in three patients. In one patient, only ill-defined hyperdensity was noted in the affected basal ganglia. Correlative MRI brain studies showed similar findings of large solid cystic masses in three patients, whereas the fourth patient showed small hyperintensities on T_2 weighted and fluid-attenuated inversion-recovery sequences. All lesions were confirmed to be germinomas on biopsy. Chemotherapy followed by radiotherapy was given to three patients. There was a dramatic response, with complete resolution of tumour bulk in two patients and >80% reduction in tumour bulk in one patient. Debulking surgery was performed in one subject who had received cranial radiotherapy; the last follow-up MRI showed no evidence of residual disease.

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Germinomas are the most common tumour among germ cell neoplasms [1]. The usual sites of intracranial germ cell tumours include the pineal and suprasellar-sellar regions. Germinoma arising from the basal ganglia, also known as ectopic germinoma, is a rare entity representing 5–10% of all intracranial germinomas [2]. A higher incidence is seen in Asian populations, with a male predominance [1]. It usually occurs in the second decade of life. Some patients have a protracted clinical presentation, which can lead to delayed diagnosis. The major signs and symptoms include progressive hemiparesis, cognitive decline and psychosis. Although rare, atypical symptoms such as precocious puberty, diabetes insipidus, speech disturbance, oculomotor palsy and hemianopsia have been described in the literature [1], but are more often seen in germ cell tumours arising from the pineal and suprasellar regions. There is an association between ipsilateral cerebral and brain stem atrophy and basal ganglia germinomas, which are found on CT and MRI in up to 33% of cases [3] and may correlate with clinical features [2].

In this pictorial review, we describe the clinical presentation, imaging findings and treatment response in four Chinese adolescent patients (three males, one

female; age range, 10–15 years; mean age, 12.5 years) who presented to our Children Cancer Center with histological proof of germinoma in the basal ganglia during the past five years.

Case 1

An 11-year-old boy presented initially with left upper limb clumsiness, frequent falls and occasional headache. Initial unenhanced CT of the brain showed a subtle hyperdensity measuring approximately 2.0 cm with a few specks of calcification in the right lentiform nucleus and cerebral peduncle (Figure 1a). A subsequent MRI showed subtle T_2 hyperintensity in the right internal capsule, putamen and thalamus, extending to the right cerebral peduncle, with an overall extent of 2.0 cm (Figure 1b). There was no enhancement on post-gadolinium contrast-enhanced images. These changes showed restricted diffusion on diffusion-weighted imaging. MR proton spectroscopy revealed normal N-acetylaspartate (NAA) and choline levels. The diagnosis was unclear at that juncture (with differential diagnoses of demyelination, vasculitis or encephalitis). However, his symptoms progressed gradually to involve the left lower limb, resulting in hemiparesis seven months later. Follow-up CT showed persistent hyperdensity with mild mass effect. Biopsy confirmed the diagnosis of basal ganglia germinoma. Serum α -fetoprotein (AFP) and human chorionic gonadotrophin (HCG) levels were normal.

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Figure 1. An 11-year-old boy presented initially with left upper limb clumsiness. (a) Unenhanced CT brain axial image shows a subtle hyperdensity (white arrow) in the right basal ganglia and cerebral peduncle without mass effect. Note the few specks of calcification (black arrow). (b). Axial T_2 weighted brain MRI reveals a subtle T_2 hyperintensity in the right internal capsule, putamen and thalamus, extending to the right cerebral peduncle (white arrow).

Serial MRI after completion of four courses of systemic chemotherapy, according to a French Society of Paediatric Oncology (SFOP) [4] chemotherapy protocol (see Appendix 1), showed complete remission. However, his neurological symptoms persisted with left upper limb weakness (Grade 4/5 over proximal muscles; Grade 3/5 over distal muscles).

Case 2

A 15-year-old boy presented with headache and vomiting of 10 days' duration. Initial unenhanced brain CT revealed a 5.0×4.5 cm right basal ganglia heterogeneous tumour with calcification, cysts and haemorrhage (Figure 2a). MRI of the brain showed a T_1 weighted and T_2 weighted mixed intensity mass in the right basal ganglia (Figure 2b). Post-gadolinium contrast-enhanced images revealed a large enhancing component (Figure 2c). No drop metastasis was identified on spinal MRI. His AFP level was normal but his HCG level was 40 IU l^{-1} (normal, $<2 \text{ IU l}^{-1}$). Biopsy confirmed germinoma. Diagnostic lumbar puncture revealed the presence of germinoma cells. In accordance with the SFOP protocol, the patient was treated for disseminated disease with four courses of systemic chemotherapy. Serum HCG levels normalised after the first course of chemotherapy. Follow-up MRI 3 months later showed a further reduction in the size of the tumour but not to the targeted complete remission or minimal residual disease level. In view of the technical difficulty encountered for repeat excision biopsy, he was treated as "partial response". Craniospinal radiotherapy (24 Gy) with an involved field boost up to a total of 45 Gy was given. Treatment has now been complete for 6 months.

The most recent MRI study showed a residual lesion with $>80\%$ reduction in volume compared with the baseline study. No residual neurological deficit was noted.

Case 3

An 11-year-old boy presented with a history of right hand clumsiness of two months' duration. Serum and cerebrospinal fluid (CSF) AFP and HCG levels were not elevated. Initial CT of the brain revealed a well-circumscribed lobulated 3.5 cm hyperdense mass lesion in the left basal ganglia, with internal solid cystic components (Figure 3a). MRI showed a lobulated T_1 weighted isointense and T_2 intermediate-to-hyperintense mass in the left basal ganglia and anterior limb of the left internal capsule with intralesional solid cystic components (Figure 3b). Post-gadolinium contrast-enhanced images revealed a similar enhancement pattern to Case 2. Brain biopsy confirmed germinoma. The patient received four courses of chemotherapy. Follow-up MRI showed a residual 4 mm enhancing nodule. Excision biopsy showed only gliotic brain tissue. Adjuvant reduced-dose craniospinal radiotherapy (30 Gy) was then given, and the treatment has been complete for one year. The most recent MRI study showed no evidence of residual disease. He had residual right-side weakness (Grade 4) with brisk reflexes.

Case 4

A 13-year-old girl presented with left hand spasm and clumsiness of four months' duration. There was gradual

Figure 2. A 15-year-old boy presented with headache and vomiting of 10 days' duration. (a) Unenhanced axial brain CT image reveals a large well-circumscribed heterogeneous tumour in the right basal ganglia. Note the speckled dense calcification (white arrow), cysts (black arrow) and haemorrhage (curved arrow). (b) Axial T_2 -weighted brain MRI shows a mixed intensity mass in the right basal ganglia with intralesional haemorrhage and cysts. Note the ill-defined T_2 hypointense areas representing calcification (white arrow). There is minimal surrounding vasogenic oedema despite the large size of the tumour. (c) T_1 weighted post-gadolinium contrast-enhanced axial image shows a large enhancing component of the right basal ganglia mass (white arrow).

progression of symptoms with involvement of the left lower limb. Initial unenhanced brain CT revealed a complex lesion (4.0×4.2 cm) with solid cystic components in the right basal ganglia (Figure 4a). Subsequent MRI showed a large T_1 weighted hypointense and T_2 intermediate-to-hyperintense lesion mass in the right basal ganglia, with solid and multicystic components (Figure 4b) and rim enhancement after gadolinium

injection. MRI study also revealed ipsilateral hemisencephalic atrophy (Figure 4c). AFP and HCG levels were normal. Debulking surgery was performed and histology confirmed a non-secreting germinoma. Only cranial radiotherapy was administered. The latest MRI 1 year after treatment showed no residual lesion. She had nearly complete neurological recovery with just mild clumsiness over the left side.

Figure 3. An 11-year-old boy presented with a history of right hand clumsiness of two months' duration. (a) Unenhanced axial brain CT reveals a large lobulated hyperdense lesion in the left basal ganglia. Note the solid haemorrhagic (white arrow) and cystic (black arrow) components. (b) Axial T_2 weighted brain MRI image shows a lobulated T_2 intermediate-to-hyperintense mass in the left caudate and anterior limb of the left internal capsule. Note the small internal cystic components (white arrow). (c) T_1 weighted post-gadolinium contrast-enhanced axial image shows intense enhancement of the solid component (white arrow) of the tumour while the small cystic components remain hypointense.

Discussion

Although an atypical entity, small case series of germinomas in the basal ganglia and thalamus have been described for Asian populations [1]. These tumours most commonly occur in patients aged 7–20 years, with a striking (20:1) male predominance [1]. Our study on a Chinese population also showed a similar demographic distribution.

Most germinomas are unilateral. As predicted by its specific site, patients with unilateral germinoma of the basal ganglia or thalamus often present with weakness or clumsiness of the extremities, with gradual progression to hemiparesis. The clinical course is usually slow, with the duration of clinical symptoms ranging from 1 month to 4.5 years [1]. Diagnosis of basal ganglionic germ cell tumours at an early stage can be difficult owing to the insidious onset of neurological deficits. Imaging is the

Figure 4. A 13-year-old girl presented with left hand spasm and clumsiness of four months' duration. (a) Unenhanced axial brain CT image shows a well-circumscribed large complex lesion in the right basal ganglia. Note the smaller haemorrhagic (white arrow) and larger cystic (black arrow) components in the right basal ganglia. (b) Axial T_2 weighted brain MRI image shows a hyperintense multiloculated mass in right basal ganglia. Note the multicystic (black arrow) components. There is minimal associated vasogenic oedema. (c) Axial T_2 weighted brain MRI image taken at a section below the basal ganglia. Note the right hemisencephalic atrophy (white arrow).

first clue to diagnosis. However, to derive an early diagnosis, it is mandatory to recognise the subtle findings of basal ganglionic germ cell tumours. In the early stage of basal ganglionic germinoma, CT may be normal, despite the presence of neurological symptoms [5, 6]. Early CT features that have been described include an irregularly defined, homogeneous or inhomogeneous, iso-attenuated to slightly hyperattenuated area without

mass effect [6–8]. A few studies have described the early MR findings of basal ganglionic germinoma. In the report of Okamoto et al [8], high T_1 signal intensity and small T_2 hyperintense lesions were seen in the basal ganglia in their two patients with germinoma. Kim et al [2] reported low signal intensity on T_1 weighted images and high signal intensity on T_2 weighted images in their two patients with small basal ganglia germinomas. These

tumours usually show no enhancement or only subtle enhancement on post-contrast T_1 weighted images in the early stages [2, 7, 8]. In this cohort, Case 1 also presented with subtle hyperdensity on CT. A correlative MR study showed patchy T_2 and fluid-attenuated inversion-recovery (FLAIR) hyperintensity in a more extended area involving the putamen, internal capsule and extending into the cerebral peduncle. The diagnosis was delayed because of the unfamiliar features of this tumour to the radiologists and clinicians.

In the more advanced stages of the disease, basal ganglionic germinoma usually presents as an irregular solid area with cystic components and variable contrast enhancement on CT and MRI [1, 2, 5–10]. Despite the size of the tumour, surrounding oedema is usually minimal, whereas mass effect onto adjacent structures is mainly caused by the primary tumour. Intratumoral haemorrhage is not uncommonly found on MR images [2, 7, 9]. On CT scans, the solid area is usually iso- or hyper-attenuated. Intralesional calcification is a frequently observed finding [1, 5–7, 9]. In our study, three out of four patients showed similar cystic changes and solid enhancing areas. Two out of four patients revealed small intratumoral speckled calcification.

The main radiological differentials for basal ganglia germinomas include glioma and lymphoma, and sometimes it is difficult to differentiate these entities on the basis of imaging findings alone. Assays of serum and CSF for tumour markers are helpful to derive the correct diagnosis [11]. Generally, in their initial stages, germinoma and lymphoma are of high density on unenhanced CT scans, whereas low-grade glioma is usually isodense to hypodense. With progression and emergence of a predominantly solid component, it is more difficult to distinguish between germinomas, malignant gliomas and lymphoma, all of which are isodense to hyperdense on unenhanced CT scans. Owing to the high cellularity and relatively low water content, these tumours appear relatively isointense on all MR pulse sequences [12]. Cystic changes, intratumoral haemorrhage and a heterogeneous pattern of contrast enhancement are more frequently seen in germinomas and gliomas. However, despite the large size, peritumoral oedema and mass effect are usually milder in germinomas than in gliomas of a similar size. Ipsilateral hemimesencephalic atrophy is also a feature of germinomas of the basal ganglia. In subsequent follow-up imaging for disease monitoring, germinomas usually show a remarkable response to chemotherapy and radiotherapy, with complete or near complete regression of the tumour bulk after treatment.

Germinomas respond readily to chemotherapy and radiotherapy, leading a good prognosis and high chance of survival for these patients. In our cohort, all patients had complete or near complete remission of the primary tumour, with a long survival outcome. Some patients even had complete neurological recovery. However, if the diagnosis is delayed, the disease can become disseminated by local or CSF spread, similar to germinomas elsewhere in the pineal or suprasellar region. Early imaging and a biopsy-based diagnosis is thus important to determine early treatment for patients with basal ganglia germinoma and to help minimise any associated neurological deficits.

Conclusions

Germinoma of the basal ganglia commonly occurs in adolescents, with distinct neurological and radiological presentations. Imaging features of these tumours include T_1 hyperintensity, flecked or amorphous calcifications, cystic areas and minimal peritumoral oedema, despite the large heterogeneously enhancing solid portion. Ipsilateral hemimesencephalic atrophy is an accompanying feature and should always be looked for. Our pictorial review may help radiologists to diagnose such basal ganglia lesions in adolescents with progressive neurological deficits, avoiding a delay in management of an otherwise prognostically favourable entity.

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Appendix 1

French Society of Pediatric Oncology (SFOP) Treatment Protocol [4]

Course 1 and 3 consisted of carboplatin (600 mg m^{-2}) on day 1 and etoposide (150 mg m^{-2} per day) from days 1 to 3.

Course 2 and 4 consisted of ifosfamide (1.8 g m^{-2} per day from days 1 to 5) and etoposide (150 mg m^{-2} per day from days 1 to 3). Each course of chemotherapy is given once every 3 weeks when the absolute neutrophil count is greater than $1 \times 10^9 \text{ l}^{-1}$ and platelet count is greater than $100 \times 10^9 \text{ l}^{-1}$. The response was assessed by imaging after two courses of chemotherapy (lumbar puncture is repeated for assessing cytology, HCG and AFP if the initial results were abnormal). Radiotherapy is given after four courses of chemotherapy. The dose of radiotherapy depends on the disease status after four courses of

chemotherapy. For patients with complete response or minimal residual disease, 30 Gy is given (local disease, 30 Gy to involved field; disseminated disease, craniospinal 21 Gy + involved field 9 Gy; occult multifocal, ventricular 21 Gy + involved field 9 Gy). For patients with partial response, stable disease or progressive disease, re-operation should be seriously considered; if the histology confirms germinoma, 45 Gy should be given (local disease, ventricular 24 Gy + involved field 21 Gy; disseminated disease, craniospinal 24 Gy + involved field 21 Gy; occult multifocal, ventricular 24 Gy + involved field 21 Gy).